

CLAIMS

1. A process for the production of inactivated Hepatitis A virus substantially free of host cell contamination, the process comprising:
- 5 a) a culturing Hepatitis A virus and harvesting a hepatitis A preparation
b) treating said hepatitis A preparation with a protease, thereafter
c) separating intact virus from protease-digested protein
d) inactivating said virus.
- 10 2. A process as claimed in claim 1 wherein the Hepatitis A virus is derived from HM-175 strain.
3. A process as claimed in claim 1 or claim 2 wherein the protease is trypsin.
- 15 4. A process as claimed in any one of claims 1 to 3 wherein part c) includes a permeation chromatography step.
5. A process as claimed in any one of claims 1 to 4, further comprising an ion exchange step after protease digestion.
- 20 6. An inactivated Hepatitis A virus obtained by the process according to any one of claims 1 to 5.
7. An inactivated Hepatitis A virus preparation substantially free of host cell
- 25 contaminants.
8. The inactivated Hepatitis A virus of claim 7, comprising less than 10% or less than 8% or less than 5% contaminating host cell proteins detectable by scanning SDS

10. A vaccine according to claim 9 formulated with a Th1-type inducing adjuvant.
11. A vaccine according to claim 10 wherein the adjuvant comprises monophosphoryl lipid A or a derivative thereof.
- 5
12. A vaccine according to claim 11 further comprising QS21.
13. A vaccine according to claim 12 further comprising an oil in water emulsion and tocopherol.
- 10
14. A vaccine according to any one of claims 9 to 13 further comprising a hepatitis B antigen.
- 15
15. A vaccine according to any one of claims 9 to 14 further comprising a non-hepatitis antigen.
16. A method of producing a hepatitis a vaccine, which method comprises mixing a preparation of inactivated hepatitis A virus according to any one of claims 6 to 8 with a pharmaceutically acceptable carrier.

Akd
A.